Marked-up Version of Amended Specification Pursuant to 37 C.F.R. §§ 1.121(b)-(c)

METHODS FOR TREATING CELLS

Mailed up version

Priority Claim

This application claims priority under 35 U.S.C. § 119 to Great Britain Application No. 0013817.2, filed June 6, 2000.

Field of the invention

This invention relates to methods for treating cells, e.g. proliferating cells, for example hyperproliferating cells, such as tumour cells, so as to damage them or reduce their proliferation.

Background of the invention and prior art

Administration to mammals of cytokines is known as such, but is often poorly tolerated by the host (A Mire-Sluis, TIBTech Vol. 11 (1993); MS Moore, Ann Rev Immunol 9 (1991), 159-191).

It is also known to modify live virus vectors to carry genes encoding a cytokine or tumour antigen, see e.g. WO 96/26267 (Cantab Pharmaceuticals: Inglis et al) and references cited therein including WO 94/16716 (Virogenetics Corporation: Paoletti et al.).

Gene sequences of a large number of cytokine genes and other immunomodulatory proteins are known. For example, human GM-CSF and its gene are described in M Cantrell et al., Proc. Nat. Acad. Sci. 82 (1985), pp 6250-6254; F Lee et al., Proc. Nat. Acad. Sci. 82 (1985), pp 4360-4364 and G Wong et al., Science 228 (1985), pp 810-815. The gene encoding murine GM-CSF is also known (Gough et al.,

Virus vectors which are defective in respect of a gene essential for production of infectious virus, such that the virus can infect normal host cells and undergo replication and expression of viral antigen genes in such cells but cannot produce infectious virus are known and described in specification WO 92/05263 (Immunology Limited: Inglis et al) and WO 94/21807 (Cantab Pharmaceuticals Research Limited: Inglis et al).

WO 92/05263 (Immunology Limited: Inglis et al) particularly describes an HSV virus which is disabled by functional deletion of a gene encoding the essential glycoprotein (gH) which is required for virus infectivity.

It is also known to administer dendritic cell preparations to mammals. BM Colombo et al. (Immunology, 2000, 99 (1): 8-15) describes vaccination of mice with tumour extract-loaded dendritic cells and subsequent generation of a CD-4 antigen specific cell-mediated cytotoxic protective immune response.

It is also known that certain bacteria can possess anti-tumour activity. H Akaza et al.(Cancer, 1993, 72 (2): 558-563) describes the anti-tumour effects of Bacillus Calmette-Guerin (BCG) against urinary bladder cancer.

[Summary and description of the invention]

Summary

According to an aspect of the invention there is provided a combination treatment for treating target cells, for example proliferating cells, e.g. hyperproliferating cells, e.g. tumour cells. The treatment comprises the steps of:

a) exposing target cells to a cell-damaging agent, for example, an agent which is capable of producing cell inflammation and/or lysis,

b) exposing said target cells to a preparation of antigen-presenting cells, e.g. dendritic cells. The cell-damaging agent can contact the target cells, or can enter, or be taken up by them. This can enable the antigen-presenting cells to encounter substances such as antigens, that can be produced by exposure of the target cells to the cell-damaging agent in step a) of the process.

In alternative embodiments, step b) can precede step a) or be carried out at the same time as step a).

Detailed Description

The invention provides in one aspect a method of treating target cells to damage them and/or reduce their proliferation: the method comprises the steps of (a) exposing the target cells to a cell-damaging agent, and also (b) exposing said target cells to a preparation of antigen-presenting cells, thereby to damage said cells and/or reduce their proliferation. Step (b) can be carried out after step (a), e.g. at least about 30 minutes after step (a). The antigen-presenting cells can consist essentially of dendritic cells. The cell-damaging agent can consist essentially of a vector, e.g. a virus vector, for gene delivery. The damage produced by the agent can be indirect, e.g. by the immune response generated. Such a virus vector can comprise one or more gene sequences encoding an immunomodulatory protein and/or a tumour antigen, or a functional fragment thereof. The cell-damaging agent and the antigen-presenting cells can be delivered to target cells in vivo, or alternatively to in-vitro cells, in which case the treated target cells can then be implanted or administered into a subject.

Thus in one form of embodiment, a method of treating cell proliferation in a subject can comprise administering to said subject separately or concurrently a preparation (a) which consists essentially of a cell-damaging agent, and a preparation (b) which consists essentially of an antigen-presenting cell preparation, in combination with a pharmaceutical excipient.